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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,825	12/23/1999	SHUN Y. LIN	2092/OG278	7998

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EXAMINER
WELLS, LAUREN Q

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/471,825	LIN ET AL.	
	Examin r	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *3-5,11,30-32,39,48,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6-10, 12-29, 33-38, 40-47, 49-53, 56-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-67 are pending. Claims 3-5, 11, 30-32, 39, 48, and 54-55 are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 9/10/02, Paper No. 20, amended claims 1, 7-8, 56, 65, 66, and added claim 67.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/10/02 has been entered.

Election/Restrictions

A call to Andrea Colby on 10/22/02, confirmed that Applicant will continue to prosecute with traverse, Group I, and the elected species, of Paper No. 8, wherein the active agents for the fast release and sustained release layer is metronidazole, wherein the water soluble polymer is hydroxypropylmethylcellulose, wherein the fatty acid is hydrogenated vegetable oil, and wherein the matrix forming agent is a combination of gelatin, xantham, polyacrylic acid polymers crosslinked with polyalkenyl polyethers and amino acids. See the Election/Restriction requirement, Paper No. 5, and the Response to Election/Restriction, Paper No. 8.

Applicant's elected species were searched. The search was not extended because prior art was found to render the species obvious.

Claim Objections

Claim 56 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The term "vegetable protein derivatives" in claims 27 (line 2), 65 (part (b)(i)) is vague and indefinite, as it is not clear what compounds are encompassed by this phrase. The specification does not define this phrase and one of ordinary skill in the art would not be apprise of its meaning.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-9, 13-15, 19-20, 22, 24-29, 37, 45-46, 49-53, 56-60, 63, 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Huber (4,122,157).

Huber teaches nitrofurantoin sustained release tablets. Exemplified is a tablet comprising a rapid release layer and a slow release layer, wherein the rapid release layer comprises 33% nitrofurantoin and 67% inert pharmaceutical excipients, and the slow release layer comprises 36% nitrofurantoin, 31% hydroxypropylmethylcellulose, and 33% inert pharmaceutical excipients. Diluents, binders, lubricants, disintegrating agents, coloring agents, and flavoring agents are disclosed as pharmaceutical excipients. Binders (matrix forming agents) disclosed for use in the fast release layer are starch, gelatin, sucrose, dextrose, molasses, acacia, sodium alginate, carboxymethylcellulose and polyvinylpyrrolidone. Hydrogenated vegetable oil is disclosed as a lubricant. In the claims, hydroxypropyl methylcellulose is disclosed as comprising 14-42% of the tablet. Thus, Huber and the instant invention both teach composition comprising a sustained release layer and a fast release layer, wherein the slow release layer comprises 31% of a water-soluble polymer (hydroxypropylmethylcellulose), hydrogenated vegetable oil and 36% of an active agent (nitrofurantoin), and the fast release layer comprises matrix forming agents (binders, such as gelatin and starch), and 33% of an active agent (nitrofurantoin). See Col. 1, line 6-Col. 7, line 35.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6, 7-10, 13-27, 29, 37-38, 41-43, 45-47, 49-53, 56-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saslawski et al. (WO 99/33448).

The instant invention is directed to a composition comprising a sustained release layer and a fast release layer, wherein the sustained release layer comprising a water-soluble polymer and an active agent, and the fast release layer comprises a matrix forming agent and an active agent, wherein the composition is freeze-dried and lyophilized.

Saslawski et al. teach a tablet for the instant and prolonged release of one or more active substances. Exemplified is a tablet, wherein the immediate release granule comprises 94.12% EMP (active agent), 2.94%polyvinylpyrrolidone 30, 2.94% cross-linked carboxymethylcellulose (matrix forming agent), and the prolonged release granule comprises 71.7% EMP, 17.2% lactose powder, 8.8% Eudragit NE, 1.10% talc, 1.2% magnesium stearate. Additives disclosed for addition to the immediate release layer include disintegrating agents, diluents, binders, lubricants, antioxidants, colourings, sweeteners, and others are disclosed. Additives disclosed for addition to the prolonged release layers include those for use with the immediate release layers, excluding disintegrating agents. Guar gum, sodium alginate, and others are disclosed as disintegrating agents that comprise 0-15% of the layer. Hydroxypropylcellulose is disclosed as a binder that can comprise 0.5-25% of the layer. Hydrogenated vegetable oils are disclosed as diluents. Miconazole, benzodiazepines such as lorazepam, are disclosed as additional active

agents, and the active agents are disclosed as comprising from 1-99% of the layers. The reference lacks an exemplification of a water-soluble polymer in the prolonged release granule. See pg. 2, line 19-pg. 12, line 38.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify the prolonged release granule of Example 1 of Saslawski et al. as further comprising hydroxypropylmethylcellulose because on page 12 of the specification Saslawski et al. teach that binders such as. . .hydroxypropylmethylcellulose. . .may be incorporated into the prolonged-release layer; thus, one of skill in the art would have been motivated to exemplify hydroxypropylmethylcellulose in the prolonged release granule of Example 1 of Saslawski et al. because of the expectation of increasing the cohesion of the granule.

Claims 12 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saslawki et al. as applied to claims 1-2, 6, 7-10, 13-27, 29, 37-38, 41-43, 45-47, 49-53, 56-67 above, and further in view of Morella et al. (5,378,474).

Saslawski et al. is applied as discussed above. The reference lacks metronidazole.

Morella et al. teaches sustained release pharmaceutical compositions having a core element and a core coating. Antibiotics disclosed for use as active agents include nitrofurantoin and metronidazole. See Col. 2, line 27Col. 5, line 45; Col. 13, line 65-Col. 15, line 21.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach metronidazole as the active agent in Saslawski et al. because a) Morella et al. and Saslawski et al. are both directed to sustained release tablets; b) Saslawski et al. teach antibiotics such as penicillin as active agents in his compositions and Morella et al. teach penicillin and metronidazole as interchangeable antibiotics for use in controlled release tablets;

thus, one of skill in the art would have been motivated to substitute metronidazole for penicillin in the tablets of Saslawski et al.

Claims 28, 33-35, 36, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saslawski et al. as applied to claims 1-2, 6, 7-10, 13-27, 29, 37-38, 41-43, 45-47, 49-53, 56-67 above, and further in view of Gole et al. (5,558,880).

Saslawski et al. is applied as discussed above. The reference lacks a matrix forming agent consisting of xanthan gum, gelatin, and amino acids.

Gole et al. teaches pharmaceutical dosage forms defined by a matrix containing gelatin, pectin and one or more amino acids having form about 2 to 12 carbon atoms. Amino acids disclosed include glycine, alanine, aspartic acid, glutamic acid, hydroxyproline, isoleucine, leucine, and phenylalanine. Other matrix forming agents disclosed include gelatins and xanthan gums. It is further disclosed that polysaccharide complexes may be utilized as matrix forming agents. The matrix materials are disclosed as comprising 0.1-15% of the total solution. See Col. 2, line 40-Col. 8, line 55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the matrix of Gole et al. to the immediate-release granule of Saslawski et al. because a) Gole et al. and Saslawski et al. are both directed to pharmaceuticals that provide immediate release of an active agent; b) Saslawski et al. teach many of the matrix components of Gole et al. as disintegrating agents for use in their immediate release layer; c) Gole et al. his matrices as resisting disintegration under manufacturing and handling, and as exhibiting a fast speed of dissolution upon ingestion; thus, one of skill in the art would be motivated to add the matrix of Gole et al. to the immediate release granule of Saslawski et al. because of the

expectation of producing a tablet that resists disintegration under manufacturing and handling and exhibits a fast speed of dissolution upon ingestion.

Claims 10, 12, 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubber et al. as applied to claims 1, 2, 6-9, 13-15, 19-20, 22, 24-29, 37, 45-46, 49-53, 56-60, 63, 65 above, and further in view of Morella et al.

Hubber et al. is applied as discussed above. The reference lacks metronidazole.

Morella et al. teaches sustained release pharmaceutical compositions having a core element and a core coating. Antibiotics disclosed for use as active agents include nitrofurantoin and metronidazole. See Col. 2, line 27Col. 5, line 45; Col. 13, line 65-Col. 15, line 21.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute metronidazole for nitrofurantoin in Hubber et al. because a) Hubber et al. and Morella et al. are both directed to sustained release tablets; b) Hubber et al. teach antibiotics such as nitrofurantoin as active agents in his compositions and Morella et al. teach nitrofurantoin and metronidazole as interchangeable antibiotics for use in controlled release tablets; thus, one of skill in the art would have been motivated to substitute metronidazole for nitrofurantoin in the tablets of Morella et al.

Claims 33-35, 36, 41-44, 64, 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubber et al. as applied to claims 1, 2, 6-9, 13-15, 19-20, 22, 24-29, 37, 45-46, 49-53, 56-60, 63, 65 above, and further in view of Gole et al.

Hubber et al. is applied as discussed above. The reference lacks matrix agents consisting of gelatin, xanthan gum, and amino acids.

Gole et al. is applied as discussed above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the matrix of Gole et al. to the fast release portion of Hubber et al. because a) Gole et al. and Hubber et al. are both directed to pharmaceuticals that provide immediate release of an active agent; b) Hubber et al. teach many of the matrix components of Gole et al. as disintegrating agents for use in their fast release portion; c) Gole et al. his matrices as resisting disintegration under manufacturing and handling, and as exhibiting a fast speed of dissolution upon ingestion; thus, one of skill in the art would be motivated to add the matrix of Gole et al. to the fast release portion of Hubber et al because of the expectation of producing a tablet that resists disintegration under manufacturing and handling and exhibits a fast speed of dissolution upon ingestion.

Claims 16-18, 21, 23, 47 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubber et al. as applied to claims 1, 2, 6-9, 13-15, 19-20, 22, 24-29, 37, 45-46, 49-53, 56-60, 63, 65 above, and further in view of Saslawki et al.

Hubber et al. is applied as discussed above. The reference lacks preferred percent weights of fatty acids and active ingredients.

Saslawski et al. is applied as discussed above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the percent weights of fatty acids and active agents taught by Saslawki et al. into the invention of Hubber et al. because a) both Saslawski et al. and Hubber et al. teach sustained release tablets comprising a sustained release layer comprising a water-soluble polymer and an active agent and a fast release layer comprising a matrix forming agent and an active agent; and b) it has been held that where the general conditions of a claim are disclosed in

the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Response to Arguments

Applicant's arguments with respect to claims 1, 2, 6-9, 13-20, 22-24, 27-29, 33-38, 40-47 and 49-53 have been considered but are moot in view of the new ground(s) of rejection. However, to the extent that the arguments may be relevant to the instant rejection, the Examiner will address them.

Applicant argues, "Importantly, the tablet described in Huber contains no water and thus cannot be freeze-dried. Nor does Huber suggest or describe the compositions made by freeze-drying". This argument is not persuasive. First, the Examiner respectfully points out that this argument is not commensurate in scope with the instant claims, as the instant claims are directed to a composition and not to a method of making a composition. Furthermore, it is pointed out that in product-by-process claims, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966.

Applicant argues, "Morella's tablet contains an inner core and an outer coating, the coating is formulated specifically for fast dissolution, but nowhere does it indicate that the outer coating should be utilized for fast release of drug. Furthermore, the process of making the Morella et al. product are specifically dried, which precludes its being subject to freeze-drying and lyophilization". This argument is not persuasive. Again, the Examiner respectfully points

out that this instant claims are not directed to a method of making a compositions, thus, the latter half of this argument is not commensurate in scope with the instant invention. Furthermore, the Examiner respectfully points out that Applicant has argued against the reference individually, when the rejection was made in combination. Morella was merely relied upon to teach the interchangeability of metronidazole with other antibiotics in sustained release tablet formulations.

Applicant argues, "As with other compressed tablet structures, that of Saslawski would not have been subject to freeze-drying as it has no water present in the structure". Again, the Examiner respectfully points out that in product-by-process claims, determination of patentability is based on the product itself.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
October 23, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

11/2/02